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IMMUNIZATION OF MAN WITH THE LIVE M-44 Q-FEVER VACCINE

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[Following is the translation of an article by A. N. Sterkhova, Azerbaydzhan Institute of Virology, Microbiology and Hygiene imeni Musabekova, published in the Russian-language periodical Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii (Journal of Microbiology, Epidemiology and Immunobiology), No 12, 1965, pages 48--52. It was submitted on 25 Feb 1965. Translation performed by Sp/7 Charles T. Ostertag, Jr.]

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For the first time in the Soviet Union a live vaccine against Q-fever was prepared at the Gamaleya Institute of Epidemiology and Microbiology, AMN, USSR, under the supervision of P. F. Zdrodovskiy.

The preparation is a suspension of a live egg culture of *Rickettsia burneti* variant M-44, dried under a vacuum in sterile skimmed milk. The harmlessness, reactogenicity and immunogenicity of the vaccine were checked in an extensive experiment on laboratory animals (Genig, 1960), and then its vaccination effect was tested on volunteers (Genig, 1961). On the basis of the data from the experimental investigations and the immunization test on volunteers, the author comes to the conclusion that the live vaccine from *Rickettsia burneti* M-44 when applied subcutaneously in a dose of 10^{-4} is harmless, areactogenic and sufficiently effective following a single inoculation.

In accordance with the data presented the Committee for Vaccines and Sera of the USSR Ministry of Public Health approved the live Q-fever vaccine for testing and further study in a mass inoculation experiment.

Based on the suggestion of P. F. Zdrodovskiy, we tested 2 series of live vaccine for the purpose of studying their reactogenic and immunogenic properties. We vaccinated workers at the Bakinsk Meat Packing Plant, a tanning concern, a raw hide plant, and Tannery No 1. The expediency of vaccinating these contingents was determined based on the data of serological investigations using the complement fixation reaction with Q-antigen. These were carried out in 1956--1958 and the number of infected workers comprises 4.7%. Besides this, among the workers at the meat packing plant cases of Q-fever were recorded and these were supported serologically. A serological investigation of these contingents of workers, which was carried out in 1963 in connection with the vaccination, revealed an increase in the percentage of infection from 4.7 up to 28.1. These data testify to the constant state of infection among the workers.

The inoculations were performed in accordance with the directions for the application of live M-44 vaccine.

A medical examination was performed prior to the inoculations. Personnel having contraindications were eliminated.

Simultaneously with the vaccinations 0.4 ml of blood was taken from the finger of the inoculated person and mixed with 1.8 ml of physiological solution containing 0.25% sodium citrate. Following precipitation of the erythrocytes the serum dilution was 1:10.

In the inoculated persons the reactogenicity of the vaccine was considered on the basis of subjective (state of health) and objective (temperature, reddening and infiltrate) data.

The serological reactions in the inoculated persons were studied in the complement fixation reaction prior to inoculation and in 58--84 days following inoculation. The reaction was set up with the Q-antigen obtained from the Gamalaya Institute of Epidemiology and Microbiology, AMN USSR.

Immediately before inoculation the vaccine was diluted with sterile physiological solution up to a specific concentration (10^{-4}).

The people received a single inoculation of 0.5 ml under the skin of the subscapular area, and in several cases in the area of the shoulder. All told 495 persons in ages from 15--20 up to 59 were inoculated with the live vaccine. This included 380 with a negative complement fixation reaction for Q-rickettsiosis and 115 men with a positive reaction in a titer of 1:10--1:40.

The subjects were kept under observation for 3--5 days and then we maintained contact with them for the next 2--3 months.

In accordance with the instructions a preliminary check on the reactogenicity of the vaccine was made on a limited group of people (26 men). In 9 of these complement fixing antibodies in titers of 1:10--1:40 were revealed in tests of serum taken prior to inoculation. The reaction was negative in the remainder. On the 2--4th day following inoculation all the persons of the control group were subjected to examination and a thermometer reading. Out of the 17 subjects with a negative complement fixation reaction, in 3 a weak general reaction was noted -- a one day rise in temperature up to 37.2° -- 37.5° on the 2--3rd day following inoculation. Two of these complained of a headache. There were no local reactions. Out of the 9 subjects with a positive complement fixation reaction prior to the inoculation, in one a local reaction was noted in the form of hyperemia, and an insignificant swelling of 1x1 cm. There were no complaints of malaise and headache.

The control test testified to the weak reactogenicity of the tested series of live vaccine against Q-fever and the feasibility of carrying out an extensive experiment on vaccination without preliminary serological investigations.

From 19 March through 1 April 1963, 20 workers from the raw hide plant and 109 workers from the meat packing plant were inoculated. Among these there were 15 and 52 men correspondingly with a negative complement fixation reaction prior to inoculation. On the 2--3rd day following inoculation they were subjected to examination and a thermometer check.

It can be seen from table 2 that following a single vaccination (dose - 0.5 ml, dilution 10^{-4}) in 223 (79%) of the 282 investigated, complement fixing antibodies were detected in the serum. The average titer equaled 1:26.6. Most frequently (86%) sera were encountered with titers from 1:10 to 1:80, and only in 14% were there sera with titers of 1:160.

In the group with the positive reaction prior to vaccination complement fixing antibodies were detected in 103 (90.3%). The average titer equaled 1:40 for the total number of positive results of the reaction. In comparing the titers in 103 men prior to vaccination and in 54--84 days following it the following results were obtained: In 24 the titers did not change, in 79 men the titer increased (in 46 -- by 2 times, in 18 -- by 4 times, in 10 -- by 8 times, and in 5 -- by 16 times).

The data of the serological investigation testify to the sufficiently high immunological effectiveness of the live vaccine against Q-fever, harmlessness in application (absence of allergy), and the ability to increase the intensity of immunity in persons in whose sera complement fixing antibodies to *Rickettsia burneti* were detected prior to inoculation.

Conclusions

1. In a test on humans (495 men) ~~we established~~ the weak reactogenicity of the live M-44 vaccine in a dose of 10^{-4} and its ~~good~~ immunological effectiveness; a positive result in the complement fixation reaction was obtained in $82.3 \pm 4\%$, the average titer was 1:26.6.

2. The vaccination of persons whose sera contained specific complement fixing antibodies prior to inoculation did not cause allergic reactions in them. Consequently the live M-44 vaccine against Q-fever may be used for inoculation without a preliminary serological investigation.

Literature

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TABLE 1

Reactogenicity of the live M-44 vaccine

Complement fixation reaction prior to inoculation	Number of subjects	General reaction		Local reaction	
		abs.	%	abs.	%
Negative	380	18	4.7	23	6
Positive	115	5	4.3	10	8.7
Total	495	23	4.6	33	6.6

Table 2

Results of the serological investigation of persons inoculated
with the live M-44 vaccine

Complement fixation reac- tion prior to inoculation	Number of subjects	Number of positive reactions		Number of persons with vari- ous titers of complement fixing antibodies					Aver- age titer
		abs.	%	1:10	1:20	1:40	1:80	1:160	
Negative	282	223	79	36	59	69	40	19	26.6
Positive	114	103	90.3	4	16	50	26	7	40
Total	396	326	82.3	40	75	119	66	26	26.6